# NMCP COVID-19 Literature Report #71: Friday, 02 July 2021

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL.

**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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## The Big Picture

### *News in Brief*

Three in 10 Americans think pandemic is over in U.S." (Gallup).

North Korea leader Kim Jong Un says a lapse in COVID protocols caused a 'grave incident'; considering the official stance is that there have been zero cases of COVID-19 in the country, it's unclear what exactly that means (NPR).

A new study suggests that the first COVID-19 cases may have emerged in October 2019 (Reuters; see also: PLOS Pathogens paper).

A policy brief [pdf] calls for reforms at the Assistant Secretary for Preparedness and Response (ASPR) to improve federal pandemic response (HPN).

"The COVID pandemic's lingering impact on clinical trials: Medical researchers are beginning to shift their focus away from COVID-19 — but the pandemic could continue to affect studies focused on other diseases" (Nature).

"Covid-19 made America's long-term care crisis impossible to ignore: Seniors want to age at home. But the US makes it hard" (Vox).

Podcast: "Max Roser on building the world's best source of COVID-19 data at Our World in Data" (80,000 Hours; 2h22min runtime, website includes key points and transcript).

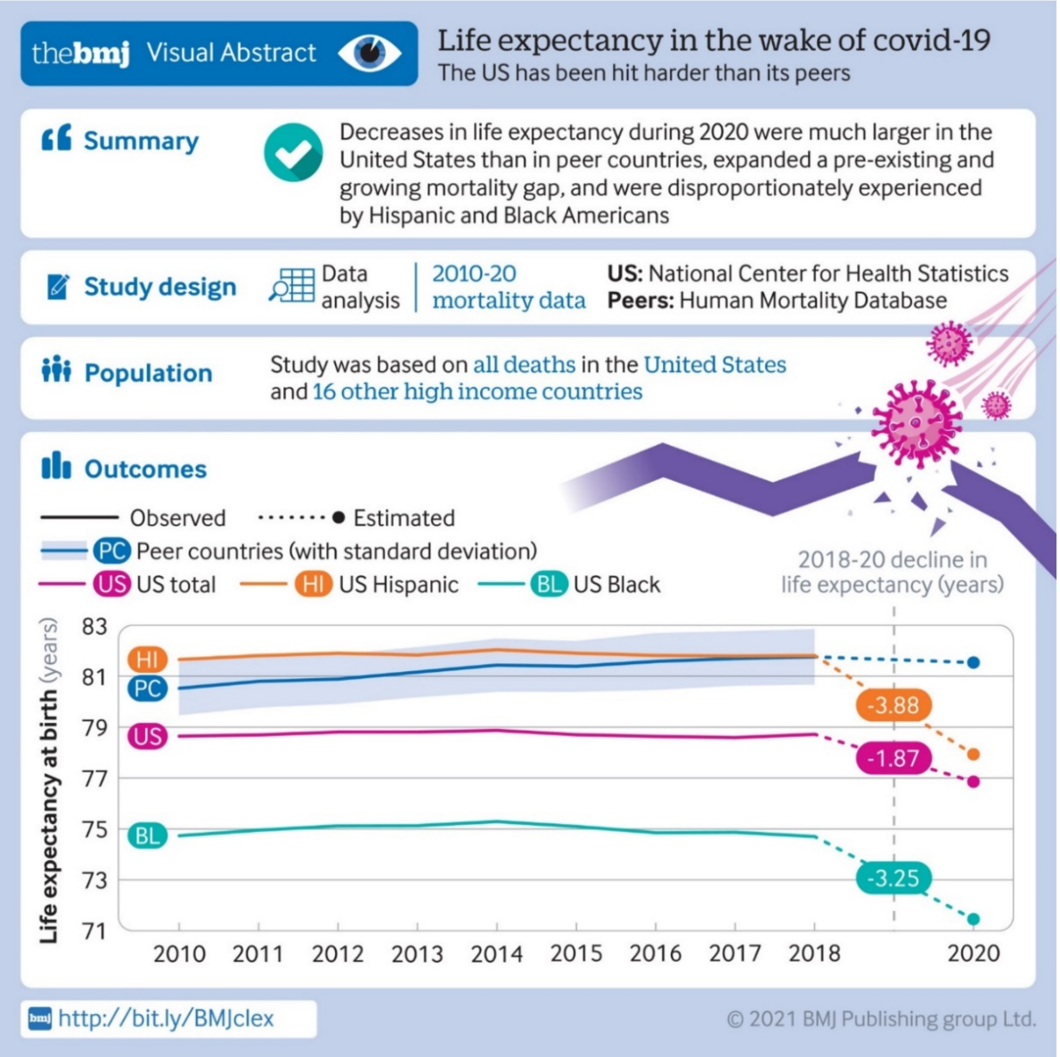
### *Peer-Reviewed Articles*

Vaccine: Increasing efficiency in vaccine Production: A primer for change (16 June 2021)

> "The COVID-19 pandemic has highlighted the importance of vaccines as public health and pandemic preparedness tools and amplified the importance of issues ranging from equitable distribution to reliable supply of quality, affordable vaccines. These issues however are not new. Delays in time from the first dose in a high-income country to introduction at scale in a low-income country can take years. These delays are driven by several challenges, some of which are unique to the vaccine development ecosystem. The patenting and overall intellectual property (IP) protection are complex, regulatory oversight is rigorous, manufacturing processes require technical support or know-how transfer from the innovator, and market dynamics create obstacles to delivering at scale. However, there are opportunities to accelerate the introduction of vaccines at scale in low and middle-income countries. To identify those opportunities, this paper provides an overview of the vaccine research and development process and where reform of the current system could increase access."

*Life Expectancy*

BMJ: [Effect of the covid-19 pandemic in 2020 on life expectancy across populations in the USA and other high income countries: simulations of provisional mortality data]() (24 June 2021)



thebmj Visual Abstract

**Life expectancy in the wake of covid-19**

The US has been hit harder than its peers

**Summary** Decreases in life expectancy during 2020 were much larger in the United States than in peer countries, expanded a pre-existing and growing mortality gap, and were disproportionately experienced by Hispanic and Black Americans

**Study design** Data analysis | 2010-20 mortality data | **US:** National Center for Health Statistics **Peers:** Human Mortality Database

**Population** Study was based on all deaths in the United States and 16 other high income countries

**Outcomes**

http://bit.ly/BMJclex

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JAMA Netw Open: [Association of the COVID-19 Pandemic With Estimated Life Expectancy by Race/Ethnicity in the United States, 2020]() (24 June 2021)

> "This cross-sectional study found that changes in life expectancy associated with COVID-19 for the total US and White populations exceeded those previously estimated. The change in life expectancy among the Black population was smaller than projected but remained much larger than that for the White population. The differences are likely partly due to the changing geography of the outbreak: since our October projections, Midwestern and Mountain states with large White populations experienced surges in COVID-19 cases and deaths. A minor change in estimates resulted from using 2018 rather than 2017 for the absent COVID-19 scenario."

## SARS-CoV-2 Virus and Variants

### *News in Brief*

*Delta, Delta, Delta (But Not the Airline, Faucet, or Sorority Versions)*

"Delta coronavirus variant: scientists brace for impact: The rapid rise of the highly transmissible strain in the United Kingdom has put countries in Europe, North America and Africa on watch" (Nature).

"Why no one is sure if delta is deadlier: The variants are spreading faster, but they don't necessarily have incentive to kill more often" (Atlantic).

"Deleted coronavirus genome sequences trigger scientific intrigue: Partial SARS-CoV-2 sequences from early outbreaks in Wuhan were removed from a US government database by the scientists who deposited them" (Nature).

"The delta variant could create 'two Americas' Of COVID, experts warn: If you are fully vaccinated, you are most likely to be safe. But in parts of the US where few people have gotten COVID vaccine shots, the Delta variant could trigger renewed deadly surges" (BuzzFeed).

*Long Reads*

"The 3 simple rules that underscore the danger of delta: Vaccines are still beating the variants, but the unvaccinated world is being pummeled" (Atlantic).

"How the delta variant is altering the course of the pandemic: The delta variant has made Covid-19 more dangerous than ever for unvaccinated people" (Vox).

### *Peer-Reviewed Articles*

Emerg Infect Dis: Predictors of Nonseroconversion after SARS-CoV-2 Infection (30 June 2021)

> "Not all persons recovering from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection develop SARS-CoV-2–specific antibodies. We show that nonseroconversion is associated with younger age and higher reverse transcription PCR cycle threshold values and identify SARS-CoV-2 viral loads in the nasopharynx as a major correlate of the systemic antibody response."

Emerg Infect Dis: Peridomestic Mammal Susceptibility to Severe Acute Respiratory Syndrome Coronavirus 2 Infection (29 June 2021)

> "Wild animals have been implicated as the origin of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but it is largely unknown how the virus affects most wildlife species and if wildlife could ultimately serve as a reservoir for maintaining the virus outside

> the human population. We show that several common peridomestic species, including deer mice, bushy-tailed woodrats, and striped skunks, are susceptible to infection and can shed the virus in respiratory secretions. In contrast, we demonstrate that cottontail rabbits, fox squirrels, Wyoming ground squirrels, black-tailed prairie dogs, house mice, and raccoons are not susceptible to SARS-CoV-2 infection. Our results expand upon the existing knowledge base of susceptible species and provide evidence that human–wildlife interactions could result in continued transmission of SARS-CoV-2."

Emerg Infect Dis: Genomic evolution of SARS-CoV-2 in immunocompromised patient, Ireland (23 June 2021)

> "We examined virus genomic evolution in an immunocompromised patient with prolonged severe acute respiratory syndrome coronavirus 2 infection. Genomic sequencing revealed genetic variation during infection: 3 intrahost mutations and possible superinfection with a second strain of the virus. Prolonged infection in immunocompromised patients may lead to emergence of new virus variants."

NEJM: SARS-CoV-2 Variants and Vaccines (23 June 2021)

> "Viral variants of concern may emerge with dangerous resistance to the immunity generated by the current vaccines to prevent coronavirus disease 2019 (Covid-19). Moreover, if some variants of concern have increased transmissibility or virulence, the importance of efficient public health measures and vaccination programs will increase. The global response must be both timely and science based."

### Vaccines and Vaccine Hesitancy

#### ***News in Brief***

"Texas man who declined COVID-19 vaccine speaks out after undergoing double lung transplant: The Texan is hoping to inspire others to get the shot now" (ABC).

Commentary: "What mRNA is good for, and what it maybe isn't" (Science).

"The mRNA vaccines are extraordinary, but Novavax is even better: Persistent hype around mRNA vaccine technology is now distracting us from other ways to end the pandemic" (Atlantic).

*Storage*

"The quest for thermostable vaccines and other innovations during Covid-19" (STAT).

"A revolutionary solar fridge will help keep COVID vaccines cold in sub-Saharan Africa" (NPR).

*Effectiveness*

Moderna says studies show its vaccine is effective against the delta variant (NPR; see also: Moderna statement).

The J&J vaccine looks to be effective against the delta variant as well (NPR; see also: J&J press release).

"CureVac COVID vaccine let-down spotlights mRNA design challenges: Scientists are searching for explanations to disappointing final-stage trial results. These insights could help guide the future development of mRNA vaccines" (Nature).

"Nearly all COVID-19 deaths in the U.S. now are in people who weren't vaccinated, a staggering demonstration of how effective the shots have been and an indication that deaths per day — now down to under 300 — could be practically zero if everyone eligible got the vaccine" (AP).

*Side Effects and Adverse Events*

"Federal health officials cite 'likely association' between coronavirus vaccines and rare heart issues in teens, young adults: They say the benefits far outweigh risks, and 'strongly encourage' vaccination for those 12 and older" (WP).

*Long Reads*

"12 lessons Covid-19 taught us about developing vaccines during a pandemic" (STAT).

"Mix-and-match COVID vaccines: the case is growing, but questions remain: A slew of studies suggests that mixing vaccines provokes potent immune responses, but scientists still want answers on real-world efficacy and rare side effects" (Nature).

## ***Special Reports and Other Resources***

KFF: KFF COVID-19 Vaccine Monitor: June 2021 (30 June 2021)

> "The KFF COVID-19 Vaccine Monitor is an ongoing research project tracking the public's attitudes and experiences with COVID-19 vaccinations. Using a combination of surveys and qualitative research, this project tracks the dynamic nature of public opinion as vaccine development and distribution unfold, including vaccine confidence and acceptance, information needs, trusted messengers and messages, as well as the public's experiences with vaccination.
>
> Key Findings
>
> - Reflecting other data indicating a slowdown in U.S. COVID-19 vaccination rates, the latest KFF COVID-19 Vaccine Monitor finds that nearly two-thirds of adults (65%) have

received at least one vaccine dose, with only a small share (3%) saying they intend to get the vaccine as soon as they can. While vaccine intentions vary by party, race, ethnicity, age, and other demographics, at least half across most demographic groups now report being vaccinated, with the exception of those who lack health insurance, 48% of whom say they have received at least one dose of a COVID-19 vaccine.

- In a new measure, we find that most adults live in homogenous households when it comes to COVID-19 vaccination status, with three-quarters (77%) of vaccinated adults saying everyone in their household is vaccinated and a similar share (75%) of unvaccinated adults saying no one they live with is vaccinated. Overall, half of adults report living in vaccinated households and one in four live in fully unvaccinated households. The remainder, about one in five adults, live in households with both vaccinated and unvaccinated household members including some households with children under the age of 12 who are not currently eligible to receive a vaccine. Notably, two-thirds of Democrats report living in all-vaccinated households while four in ten Republicans (39%) report living in all-unvaccinated homes.
- With COVID-19 case rates at record lows and much of the country re-opening, most adults (76%) are optimistic that the U.S. is nearing the end of the pandemic. However, this optimism has the potential to hamper further vaccination efforts, with half of unvaccinated adults saying that the number of cases is now so low there is no need for more people to get the vaccine.
- Consistent with last month's results, three in ten unvaccinated adults, rising to about half of those in the "wait and see" group, say they would be more likely to get vaccinated if one of the vaccines currently authorized for emergency use were to receive full approval from the FDA. However, this finding likely suggests that FDA approval is a proxy for general safety concerns, as two-thirds of adults (including a large majority of unvaccinated adults) either believe the vaccines currently available in the U.S. already have full approval from the FDA or are unsure whether they have full approval or are authorized for emergency use. In terms of other incentives and interventions, a million dollar lottery could motivate about a quarter of the unvaccinated to get a shot, while mobile vaccine clinics motivate about one in six overall, but notably higher shares of Black and Hispanic adults, suggesting such outreach could help further reduce racial and ethnic disparities in vaccination rates.
- Two-thirds of employed adults say their employer has encouraged workers to get vaccinated and half say their employer provided them paid time off to get the vaccine or recover from side effects. Notably, workers who say their employer did either one of these things are more likely to report being vaccinated, even after controlling for other demographics, suggesting that more employers encouraging vaccination and offering paid time off could lead to higher vaccination rates among U.S. workers.
- While half the public overall say employers should require their workers to get vaccinated, most workers do not want their own employer to require vaccination,

including the vast majority of unvaccinated workers (92%) as well as four in ten workers who are already vaccinated (42%). About four in ten adults say employers should provide cash bonuses or other incentives to workers who get vaccinated, but just 12% of workers say their own employer has offered such an incentive.

- Reported vaccination rates continue to increase among children ages 12-17, with one-third of parents of children in this age range saying their child has received at least one vaccine dose, up from 24% in May. However, many parents are still waiting and one-quarter say they will “definitely not” vaccinate their child. Similar to employer requirements, about half the public overall supports K-12 schools requiring COVID-19 vaccination, but most parents are opposed, with divisions along partisan lines. A somewhat larger share of the public (58%) says colleges and universities should require students to be vaccinated, including 58% of those who say they are currently undergraduate or graduate students."

## ***Peer-Reviewed Articles***

### *Vaccine Coverage*

MMWR: COVID-19 Vaccination Coverage Among Adults — United States, December 14, 2020–May 22, 2021 (21 June 2021)

> "What is already known about this topic? The U.S. COVID-19 vaccination program initially prioritized groups at highest risk for COVID-19 hospitalization and death; by April 19, 2021, eligibility expanded to all persons aged ≥16 years.
>
> What is added by this report? By May 22, 2021, 57.0% of U.S. adults aged ≥18 years had received ≥1 vaccine dose; coverage was lower and increased more slowly over time among younger adults. If the current rate of vaccination continues through August, coverage among young adults will remain substantially lower than among older adults.
>
> What are the implications for public health practice? Efforts to improve vaccination coverage are needed, especially among younger adults, to reduce COVID-19 cases, hospitalizations, and deaths."

MMWR: COVID-19 Vaccination Coverage and Intent Among Adults Aged 18–39 Years — United States, March–May 2021 (21 June 2021)

> "What is already known about this topic? Since April 19, 2021, all persons aged ≥16 years have been eligible for COVID-19 vaccination. Vaccination coverage and intent among adults are lowest among those aged 18–39 years.
>
> What is added by this report? Overall, 34% of adults aged 18–39 years reported having received a COVID-19 vaccine. Adults aged 18–24 years, as well as non-Hispanic Black adults

> and those with less education, no insurance, and lower household incomes, had the lowest reported vaccination coverage and intent to get vaccinated. Concerns about vaccine safety and effectiveness were commonly cited barriers to vaccination.
>
> What are the implications for public health practice? Addressing concerns about COVID-19 vaccine safety and efficacy and emphasizing the role of vaccination in protecting family and friends and resuming social activities might help increase coverage."

*Efficacy*

NEJM: Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines (30 June 2021)

> "Background: Information is limited regarding the effectiveness of the two-dose messenger RNA (mRNA) vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) in preventing infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and in attenuating coronavirus disease 2019 (Covid-19) when administered in real-world conditions.
>
> Methods: We conducted a prospective cohort study involving 3975 health care personnel, first responders, and other essential and frontline workers. From December 14, 2020, to April 10, 2021, the participants completed weekly SARS-CoV-2 testing by providing mid-turbinate nasal swabs for qualitative and quantitative reverse-transcriptase-polymerase-chain-reaction (RT-PCR) analysis. The formula for calculating vaccine effectiveness was 100% × (1 - hazard ratio for SARS-CoV-2 infection in vaccinated vs. unvaccinated participants), with adjustments for the propensity to be vaccinated, study site, occupation, and local viral circulation.
>
> Results: SARS-CoV-2 was detected in 204 participants (5%), of whom 5 were fully vaccinated (≥14 days after dose 2), 11 partially vaccinated (≥14 days after dose 1 and <14 days after dose 2), and 156 unvaccinated; the 32 participants with indeterminate vaccination status (<14 days after dose 1) were excluded. Adjusted vaccine effectiveness was 91% (95% confidence interval [CI], 76 to 97) with full vaccination and 81% (95% CI, 64 to 90) with partial vaccination. Among participants with SARS-CoV-2 infection, the mean viral RNA load was 40% lower (95% CI, 16 to 57) in partially or fully vaccinated participants than in unvaccinated participants. In addition, the risk of febrile symptoms was 58% lower (relative risk, 0.42; 95% CI, 0.18 to 0.98) and the duration of illness was shorter, with 2.3 fewer days spent sick in bed (95% CI, 0.8 to 3.7).
>
> Conclusions: Authorized mRNA vaccines were highly effective among working-age adults in preventing SARS-CoV-2 infection when administered in real-world conditions, and the vaccines attenuated the viral RNA load, risk of febrile symptoms, and duration of illness among those who had breakthrough infection despite vaccination."

NEJM: Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine (30 June 2021)

> "Background: Early clinical data from studies of the NVX-CoV2373 vaccine (Novavax), a recombinant nanoparticle vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that contains the full-length spike glycoprotein of the prototype strain plus Matrix-M adjuvant, showed that the vaccine was safe and associated with a robust immune response in healthy adult participants. Additional data were needed regarding the efficacy, immunogenicity, and safety of this vaccine in a larger population.
>
> Methods: In this phase 3, randomized, observer-blinded, placebo-controlled trial conducted at 33 sites in the United Kingdom, we assigned adults between the ages of 18 and 84 years in a 1:1 ratio to receive two intramuscular 5-μg doses of NVX-CoV2373 or placebo administered 21 days apart. The primary efficacy end point was virologically confirmed mild, moderate, or severe SARS-CoV-2 infection with an onset at least 7 days after the second injection in participants who were serologically negative at baseline.
>
> Results: A total of 15,187 participants underwent randomization, and 14,039 were included in the per-protocol efficacy population. Of the participants, 27.9% were 65 years of age or older, and 44.6% had coexisting illnesses. Infections were reported in 10 participants in the vaccine group and in 96 in the placebo group, with a symptom onset of at least 7 days after the second injection, for a vaccine efficacy of 89.7% (95% confidence interval [CI], 80.2 to 94.6). No hospitalizations or deaths were reported among the 10 cases in the vaccine group. Five cases of severe infection were reported, all of which were in the placebo group. A post hoc analysis showed an efficacy of 86.3% (95% CI, 71.3 to 93.5) against the B.1.1.7 (or alpha) variant and 96.4% (95% CI, 73.8 to 99.5) against non-B.1.1.7 variants. Reactogenicity was generally mild and transient. The incidence of serious adverse events was low and similar in the two groups.
>
> Conclusions: A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant."

NEJM: Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19 (10 June 2021)

> "Background: The Ad26.COV2.S vaccine is a recombinant, replication-incompetent human adenovirus type 26 vector encoding full-length severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein in a prefusion-stabilized conformation.
>
> Methods: In an international, randomized, double-blind, placebo-controlled, phase 3 trial, we randomly assigned adult participants in a 1:1 ratio to receive a single dose of Ad26.COV2.S (5×1010 viral particles) or placebo. The primary end points were vaccine efficacy against moderate to severe-critical coronavirus disease 2019 (Covid-19) with an

> onset at least 14 days and at least 28 days after administration among participants in the per-protocol population who had tested negative for SARS-CoV-2. Safety was also assessed.
>
> Results: The per-protocol population included 19,630 SARS-CoV-2-negative participants who received Ad26.COV2.S and 19,691 who received placebo. Ad26.COV2.S protected against moderate to severe-critical Covid-19 with onset at least 14 days after administration (116 cases in the vaccine group vs. 348 in the placebo group; efficacy, 66.9%; adjusted 95% confidence interval [CI], 59.0 to 73.4) and at least 28 days after administration (66 vs. 193 cases; efficacy, 66.1%; adjusted 95% CI, 55.0 to 74.8). Vaccine efficacy was higher against severe-critical Covid-19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥14 days and 85.4% [adjusted 95% CI, 54.2 to 96.9] for onset at ≥28 days). Despite 86 of 91 cases (94.5%) in South Africa with sequenced virus having the 20H/501Y.V2 variant, vaccine efficacy was 52.0% and 64.0% against moderate to severe-critical Covid-19 with onset at least 14 days and at least 28 days after administration, respectively, and efficacy against severe-critical Covid-19 was 73.1% and 81.7%, respectively. Reactogenicity was higher with Ad26.COV2.S than with placebo but was generally mild to moderate and transient. The incidence of serious adverse events was balanced between the two groups. Three deaths occurred in the vaccine group (none were Covid-19-related), and 16 in the placebo group (5 were Covid-19-related).
>
> Conclusions: A single dose of Ad26.COV2.S protected against symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection and was effective against severe-critical disease, including hospitalization and death. Safety appeared to be similar to that in other phase 3 trials of Covid-19 vaccines."

*Adverse Events and Side Effects*

JAMA Cardiol: Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military (29 June 2021)

> "Question  Should myocarditis be considered a potential adverse event following immunization with messenger RNA (mRNA) COVID-19 vaccines?
>
> Findings  In this case series of 23 male patients, including 22 previously healthy military members, myocarditis was identified within 4 days of receipt of a COVID-19 vaccine. For most patients (n = 20), the diagnosis was made after the second dose of mRNA COVID-19 vaccine; these episodes occurred against the backdrop of 2.8 million doses of mRNA COVID-19 vaccines administered.
>
> Meaning  Vigilance for rare adverse events, including myocarditis, after COVID-19 vaccination is warranted but should not diminish overall confidence in vaccination during the current pandemic."
>
> See also: editorial

JAMA Cardiol: Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination (29 June 2021)

> "Question  Is COVID-19 vaccination linked to the occurrence of myocarditis?
>
> Findings  In this study of 7 patients with acute myocarditis, 4 occurred within 5 days of COVID-19 vaccination between February 1 and April 30, 2021. All 4 patients had received the second dose of a messenger RNA (mRNA) vaccine, presented with severe chest pain, had biomarker evidence of myocardial injury, were hospitalized, and had cardiac magnetic resonance imaging findings typical of myocarditis.
>
> Meaning  Although causality cannot be established, the findings raise the possibility of an association between mRNA COVID-19 vaccination and acute myocarditis."
>
> See also: editorial

JAMA Otolaryngol Head Neck Surg: Association of COVID-19 Vaccination and Facial Nerve Palsy: A Case-Control Study (24 June 2021)

> "Question  Is the Pfizer-BioNTech BNT162b2 COVID-19 vaccine associated with increased risk of peripheral facial nerve palsy?
>
> Findings  In this case-control study of 37 patients with acute-onset facial nerve palsy and a matched control group, no increased risk of facial nerve palsy was observed after vaccination. In addition, no meaningful increase in the number of admissions for facial nerve palsy was observed compared with preceding years.
>
> Meaning  These outcomes suggest that recent vaccination with the BNT162b2 vaccine is not associated with an increased risk of facial nerve palsy."

JAMA Dermatol: Incidence of Cutaneous Reactions After Messenger RNA COVID-19 Vaccines (23 June 2021)

> "This cohort study examines cutaneous reactions in hospital employees who received messenger RNA COVID-19 vaccination....
>
> In this prospective cohort of almost 50 000 health care employees, 1.9% self-reported cutaneous reactions after receiving the first dose of an mRNA COVID-19 vaccine. With more than 600 employees with first-dose cutaneous reactions included, 83% did not have recurrent cutaneous reactions. An additional 2.3% reported cutaneous reactions only after the second dose of the vaccine.
>
> Cutaneous reactions were more commonly reported among women, which was similar to reported local injection site reactions and anaphylaxis after mRNA COVID vaccinations. To our knowledge, the underlying cause for this difference is not yet known, although drug allergies are more common in women."

Ann Neurol: Guillain-Barré Syndrome following ChAdOx1-S/nCoV-19 Vaccine (10 June 2021)

> "As of April 22, 2021, around 1.5 million individuals in three districts of Kerala, India had been vaccinated with COVID-19 vaccines. Over 80% of these individuals (1.2 million) received the ChAdOx1-S/nCoV-19 vaccine. In this population, during this period of 4 weeks (mid-March to mid-April 2021), we observed seven cases of Guillain-Barre syndrome (GBS) that occurred within 2 weeks of the first dose of vaccination. All seven patients developed severe GBS. The frequency of GBS was 1.4- to 10-fold higher than that expected in this period for a population of this magnitude. In addition, the frequency of bilateral facial weakness, which typically occurs in <20% of GBS cases, suggests a pattern associated with the vaccination. While the benefits of vaccination substantially outweigh the risk of this relatively rare outcome (5.8 per million), clinicians should be alert to this possible adverse event, as six out of seven patients progressed to areflexic quadriplegia and required mechanical ventilatory support."

Ann Neurol: Guillain-Barré syndrome variant occurring after SARS-CoV-2 vaccination (10 June 2021)

> "Whilst SARS-CoV-2 vaccines are very safe, we report four cases of the bifacial weakness with paraesthesias variant of Guillain-Barré syndrome (GBS) occurring within three weeks of vaccination with the Oxford-AstraZeneca SARS-CoV-2 vaccine. This rare neurological syndrome has previously been reported in association with SARS-CoV-2 infection itself. Our cases were given either intravenous immunoglobulin, oral steroids, or no treatment. We suggest vigilance for cases of bifacial weakness with paraesthesias variant GBS following vaccination for SARS-CoV-2 and that post-vaccination surveillance programs ensure robust data capture of this outcome, to assess for causality."

## Treatments and Management

### *News in Brief*

Symptoms of COVID-19, especially in areas where the delta variant is spreading, are starting to look more like getting a really bad cold (NBC).

The FDA issued a EUA for tocilizumab for hospitalized adult and pediatric patients (>2 yo) who are getting systemic corticosteroids and oxygen (FDA).

The NIH is ending its ACTIV-4B study looking at outpatient thrombosis prevention in COVID-19 patients; "[r]esults suggest that not treating certain symptomatic but stable outpatients with anticoagulant or antiplatelet therapy may be the best course of action" (EurekAlert).

The PRINCIPLE trial will investigate ivermectin as a possible treatment for COVID-19 (PRINCIPLE).

### *Peer-Reviewed Articles*

Anaesthesia: Factors associated with mortality in patients with COVID-19 admitted to intensive care: a systematic review and meta-analysis (29 June 2021)

> "Identification of high-risk patients admitted to intensive care with COVID-19 may inform management strategies. The objective of this meta-analysis was to determine factors associated with mortality among adults with COVID-19 admitted to intensive care by searching databases for studies published between 1 January 2020 and 6 December 2020. Observational studies of COVID-19 adults admitted to critical care were included. Studies of mixed cohorts and intensive care cohorts restricted to a specific patient sub-group were excluded. Dichotomous variables were reported with pooled OR and 95%CI, and continuous variables with pooled standardised mean difference (SMD) and 95%CI. Fifty-eight studies (44,305 patients) were included in the review. Increasing age (SMD 0.65, 95%CI 0.53-0.77); smoking (OR 1.40, 95%CI 1.03-1.90); hypertension (OR 1.54, 95%CI 1.29-1.85); diabetes (OR 1.41, 95%CI 1.22-1.63); cardiovascular disease (OR 1.91, 95%CI 1.52-2.38); respiratory disease (OR 1.75, 95%CI 1.33-2.31); renal disease (OR 2.39, 95%CI 1.68-3.40); and malignancy (OR 1.81, 95%CI 1.30-2.52) were associated with mortality. A higher sequential organ failure assessment score (SMD 0.86, 95%CI 0.63-1.10) and acute physiology and chronic health evaluation-2 score (SMD 0.89, 95%CI 0.65-1.13); a lower PaO2 :FI O2 (SMD -0.44, 95%CI -0.62 to -0.26) and the need for mechanical ventilation at admission (OR 2.53, 95%CI 1.90-3.37) were associated with mortality. Higher white cell counts (SMD 0.37, 95%CI 0.22-0.51); neutrophils (SMD 0.42, 95%CI 0.19-0.64); D-dimers (SMD 0.56, 95%CI 0.43-0.69); ferritin (SMD 0.32, 95%CI 0.19-0.45); lower platelet (SMD -0.22, 95%CI -0.35 to -0.10); and lymphocyte counts (SMD -0.37, 95%CI -0.54 to -0.19) were all associated with mortality. In conclusion, increasing age, pre-existing comorbidities, severity of illness based on validated scoring systems, and the host response to the disease were associated with mortality; while male sex and increasing BMI were not. These factors have prognostic relevance for patients admitted to intensive care with COVID-19."

Adv Sci: Combined Metabolic Activators Accelerates Recovery in Mild-to-Moderate COVID-19 (28 June 2021)

> "COVID-19 is associated with mitochondrial dysfunction and metabolic abnormalities, including the deficiencies in nicotinamide adenine dinucleotide (NAD+) and glutathione metabolism. Here it is investigated if administration of a mixture of combined metabolic activators (CMAs) consisting of glutathione and NAD+ precursors can restore metabolic function and thus aid the recovery of COVID-19 patients. CMAs include l-serine, N-acetyl-l-

> cysteine, nicotinamide riboside, and l-carnitine tartrate, salt form of l-carnitine. Placebo-controlled, open-label phase 2 study and double-blinded phase 3 clinical trials are conducted to investigate the time of symptom-free recovery on ambulatory patients using CMAs. The results of both studies show that the time to complete recovery is significantly shorter in the CMA group (6.6 vs 9.3 d) in phase 2 and (5.7 vs 9.2 d) in phase 3 trials compared to placebo group. A comprehensive analysis of the plasma metabolome and proteome reveals major metabolic changes. Plasma levels of proteins and metabolites associated with inflammation and antioxidant metabolism are significantly improved in patients treated with CMAs as compared to placebo. The results show that treating patients infected with COVID-19 with CMAs lead to a more rapid symptom-free recovery, suggesting a role for such a therapeutic regime in the treatment of infections leading to respiratory problems."

Clin Infect Dis: Ivermectin for the treatment of COVID-19: A systematic review and meta-analysis of randomized controlled trials (28 June 2021)

> "Background: We systematically assessed benefits and harms of the use of ivermectin (IVM) in COVID-19 patients.
>
> Methods: Published and preprint randomized controlled trials (RCTs) assessing IVM effects on COVID-19 adult patients were searched until March 22, 2021 in five engines. Primary outcomes were all-cause mortality, length of stay (LOS), and adverse events (AE). Secondary outcomes included viral clearance and severe AEs. Risk of bias (RoB) was evaluated using Cochrane RoB 2·0 tool. Inverse variance random effect meta-analyses were performed. with quality of evidence (QoE) evaluated using GRADE methodology.
>
> Results: Ten RCTs (n=1173) were included. Controls were standard of care [SOC] in five RCTs and placebo in five RCTs. COVID-19 disease severity was mild in 8 RCTs, moderate in one RCT, and mild and moderate in one RCT. IVM did not reduce all-cause mortality vs. controls (RR 0.37, 95%CI 0.12 to 1.13, very low QoE) or LOS vs. controls (MD 0.72 days, 95%CI -0.86 to 2.29, very low QoE). AEs, severe AE and viral clearance were similar between IVM and controls (all outcomes: low QoE). Subgroups by severity of COVID-19 or RoB were mostly consistent with main analyses; all-cause mortality in three RCTs at high RoB was reduced with IVM.
>
> Conclusions: In comparison to SOC or placebo, IVM did not reduce all-cause mortality, length of stay or viral clearance in RCTs in COVID-19 patients with mostly mild disease. IVM did not have an effect on AEs or severe AEs. IVM is not a viable option to treat COVID-19 patients."

Clin Infect Dis: Neutralizing Monoclonal Antibody Treatment Reduces Hospitalization for Mild and Moderate COVID-19: A Real-World Experience (24 June 2021)

> "Background: Neutralizing monoclonal antibody (NmAb) treatments have received emergency use authorization to treat patients with mild or moderate COVID-19 infection. To date, no real- world data about the efficacy of NmAb has been reported from clinical practice. We assessed the impact of NmAb treatment given in the outpatient clinical practice setting on hospital utilization.
>
> Methods: Electronic medical records were used to identify adult COVID-19 patients who received NmAbs [bamlanivimab (BAM) or casirivimab and imdevimab (REGN-COV2)] and historic COVID-19 controls. Post-index hospitalization rates were compared.
>
> Results: 707 confirmed COVID-19 patients received NmAb and 1709 historic COVID-19 controls were included; 553 (78%) received BAM, 154 (22%) received REGN-COV2. Patients receiving NmAb infusion had significantly lower hospitalization rate (5.8% vs. 11.4%, p<0.0001); a shorter length of stay if hospitalized (mean 5.2 days vs. 7.4 days, p=0.02), and fewer ED visits within 30 days post-index (8.1% vs 12.3%, p=0.003) than controls. Hospitalization-free survival was significantly longer in NmAb patients compared to controls (p<0.0001). There was a trend towards a lower hospitalization rate among patients who received NmAb within 2-4 days after symptom onset. In multivariate analysis, having received a NmAb transfusion was independently associated with a lower risk of hospitalization after adjustment for age, sex, race, BMI and referral source: adjusted hazard ratio (95% CI) = 0.54 (0.38 - 0.79), p=0.0012. Overall mortality was not different between the two groups.
>
> Conclusions and relevance: NmAb treatment reduced hospital utilization especially when received within a few days of symptom onset. Further study is needed to validate these findings."

Nature: In vivo monoclonal antibody efficacy against SARS-CoV-2 variant strains (21 June 2021)

> "Rapidly-emerging variants jeopardize antibody-based countermeasures against SARS-CoV-2. While cell culture experiments have demonstrated loss of potency of several anti-spike neutralizing antibodies against SARS-CoV-2 variant strains1-3, the in vivo significance of these results remains uncertain. Using a panel of monoclonal antibodies (mAbs) corresponding to many in advanced clinical development by Vir Biotechnology, AbbVie, AstraZeneca, Regeneron, and Lilly, we report the impact on protection in animals against authentic SARS-CoV-2 variants including viruses with B.1.1.7, B.1.351, or B.1.1.28 spike genes. Although some individual mAbs showed reduced or abrogated neutralizing activity in cell culture against B.1.351, B.1.1.28, B.1.617.1, and B.1.526 viruses with E484 spike protein mutations, low prophylactic doses of mAb combinations protected against infection by many variants in K18-hACE2 transgenic mice, 129S2 immunocompetent mice, and hamsters

> without emergence of resistance. Exceptions were mAb LY-CoV555 and LY-CoV555/LY-CoV016 mono- and combination therapy, which lost all protective activity, and AbbVie 2B04/47D11, which showed partial loss of activity. When administered after infection as therapy, higher doses of several mAb cocktails protected in vivo against viruses with a B.1.351 spike gene. Thus, many, but not all, of the antibody products with Emergency Use Authorization (EUA) should retain substantial efficacy against the prevailing SARS-CoV-2 variant strains."

Am J Ther: Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines (17 June 2021)

> "Background: Repurposed medicines may have a role against the SARS-CoV-2 virus. The antiparasitic ivermectin, with antiviral and anti-inflammatory properties, has now been tested in numerous clinical trials.
>
> Areas of uncertainty: We assessed the efficacy of ivermectin treatment in reducing mortality, in secondary outcomes, and in chemoprophylaxis, among people with, or at high risk of, COVID-19 infection.
>
> Data sources: We searched bibliographic databases up to April 25, 2021. Two review authors sifted for studies, extracted data, and assessed risk of bias. Meta-analyses were conducted and certainty of the evidence was assessed using the GRADE approach and additionally in trial sequential analyses for mortality. Twenty-four randomized controlled trials involving 3406 participants met review inclusion.
>
> Therapeutic advances: Meta-analysis of 15 trials found that ivermectin reduced risk of death compared with no ivermectin (average risk ratio 0.38, 95% confidence interval 0.19-0.73; n = 2438; I2 = 49%; moderate-certainty evidence). This result was confirmed in a trial sequential analysis using the same DerSimonian-Laird method that underpinned the unadjusted analysis. This was also robust against a trial sequential analysis using the Biggerstaff-Tweedie method. Low-certainty evidence found that ivermectin prophylaxis reduced COVID-19 infection by an average 86% (95% confidence interval 79%-91%). Secondary outcomes provided less certain evidence. Low-certainty evidence suggested that there may be no benefit with ivermectin for "need for mechanical ventilation," whereas effect estimates for "improvement" and "deterioration" clearly favored ivermectin use. Severe adverse events were rare among treatment trials and evidence of no difference was assessed as low certainty. Evidence on other secondary outcomes was very low certainty.
>
> Conclusions: Moderate-certainty evidence finds that large reductions in COVID-19 deaths are possible using ivermectin. Using ivermectin early in the clinical course may reduce numbers progressing to severe disease. The apparent safety and low cost suggest that ivermectin is likely to have a significant impact on the SARS-CoV-2 pandemic globally."

NEJM: Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia (16 June 2021)

> "Background: The efficacy and safety of tofacitinib, a Janus kinase inhibitor, in patients who are hospitalized with coronavirus disease 2019 (Covid-19) pneumonia are unclear.
>
> Methods: We randomly assigned, in a 1:1 ratio, hospitalized adults with Covid-19 pneumonia to receive either tofacitinib at a dose of 10 mg or placebo twice daily for up to 14 days or until hospital discharge. The primary outcome was the occurrence of death or respiratory failure through day 28 as assessed with the use of an eight-level ordinal scale (with scores ranging from 1 to 8 and higher scores indicating a worse condition). All-cause mortality and safety were also assessed.
>
> Results: A total of 289 patients underwent randomization at 15 sites in Brazil. Overall, 89.3% of the patients received glucocorticoids during hospitalization. The cumulative incidence of death or respiratory failure through day 28 was 18.1% in the tofacitinib group and 29.0% in the placebo group (risk ratio, 0.63; 95% confidence interval [CI], 0.41 to 0.97; P = 0.04). Death from any cause through day 28 occurred in 2.8% of the patients in the tofacitinib group and in 5.5% of those in the placebo group (hazard ratio, 0.49; 95% CI, 0.15 to 1.63). The proportional odds of having a worse score on the eight-level ordinal scale with tofacitinib, as compared with placebo, was 0.60 (95% CI, 0.36 to 1.00) at day 14 and 0.54 (95% CI, 0.27 to 1.06) at day 28. Serious adverse events occurred in 20 patients (14.1%) in the tofacitinib group and in 17 (12.0%) in the placebo group.
>
> Conclusions: Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo."

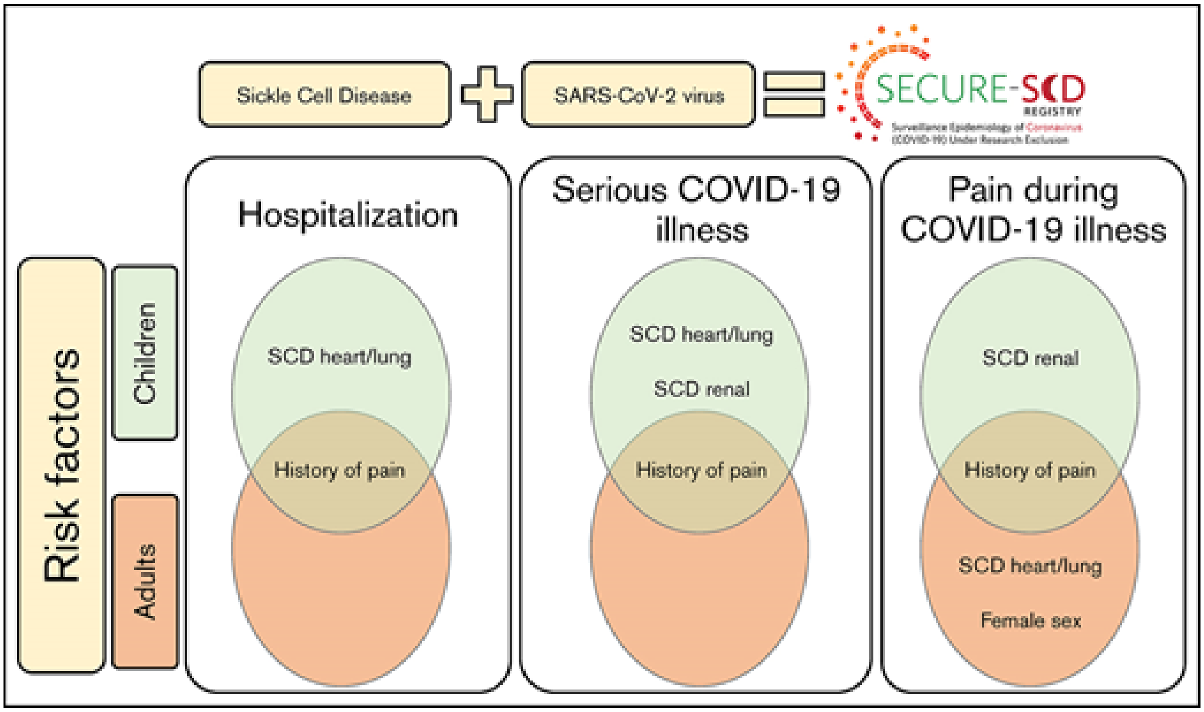
## Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

### *Peer-Reviewed Articles*

Blood Adv: Comorbidities are risk factors for hospitalization and serious COVID-19 illness in children and adults with sickle cell disease (01 July 2021)

> "Patients with sickle cell disease (SCD) are at high risk of developing serious infections, therefore, understanding the impact that severe acute respiratory syndrome coronavirus 2 infection has on this population is important. We sought to identify factors associated with hospitalization and serious COVID-19 illness in children and adults with SCD.We established the international SECURE-SCD Registry to collect data on patients with SCD and COVID-19 illness. We used multivariable logistic models to estimate the independent effects of age, sex, genotype, hydroxyurea, and SCD-related and -nonrelated comorbidities on hospitalization, serious COVID-19 illness, and pain as a presenting symptom during COVID-

> 19 illness. As of 23 March 2021, 750 COVID-19 illness cases in patients with SCD were reported to the registry. We identified history of pain (relative risk [RR], 2.15; P < .0001) and SCD heart/lung comorbidities (RR, 1.61; P = .0001) as risk factors for hospitalization in children. History of pain (RR, 1.78; P = .002) was also a risk factor for hospitalization in adults. Children with history of pain (RR, 3.09; P = .009), SCD heart/lung comorbidities (RR, 1.76; P = .03), and SCD renal comorbidities (RR, 3.67; P < .0001) and adults with history of pain (RR 1.94, P = .02) were at higher risk of developing serious COVID-19 illness. History of pain and SCD renal comorbidities also increased risk of pain during COVID-19 in children; history of pain, SCD heart/lung comorbidities, and female sex increased risk of pain during COVID-19 in adults. Hydroxyurea showed no effect on hospitalization and COVID-19 severity, but it lowered the risk of presenting with pain in adults during COVID-19."



Prev Med: [COVID-19 impact on screening test volume through the National Breast and Cervical Cancer early detection program, January–June 2020, in the United States]() (30 June 2021)

> "Women from racial and ethnic minority groups face a disproportionate burden of cervical and breast cancers in the United States. The Coronavirus Disease 2019 (COVID-19) pandemic might exacerbate these disparities as supply and demand for screening services are reduced. The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) provides cancer screening services to women with low income and inadequate health insurance. We examined COVID-19's impact on NBCCEDP screening services during January-June 2020. We found the total number of NBCCEDP-funded breast and cervical cancer

> screening tests declined by 87% and 84%, respectively, during April 2020 compared with the previous 5-year averages for that month. The extent of declines varied by geography, race/ethnicity, and rurality. In April 2020, screening test volume declined most severely in Health and Human Services Region 2 - New York (96% for breast, 95% for cervical cancer screening) compared to the previous 5-year averages. The greatest declines were among American Indian/Alaskan Native women for breast cancer screening (98%) and Asian Pacific Islander women for cervical cancer screening (92%). Test volume began to recover in May and, by June 2020, NBCCEDP breast and cervical cancer screening test volume was 39% and 40% below the 5-year average for that month, respectively. However, breast cancer screening remained over 50% below the 5-year average among women in rural areas. NBCCEDP programs reported assisting health care providers resume screening."

JAMA Dermatol: Epidemiologic Analysis of Chilblains Cohorts Before and During the COVID-19 Pandemic (23 June 2021)

> "Question  Was the incidence of chilblains correlated with the incidence of COVID-19 in the same location?
>
> Findings  In this cohort study of 1319 patients in northern California diagnosed with chilblains before and during the COVID-19 pandemic, the incidence of chilblains increased during the pandemic. However, the incidence of chilblains was only weakly correlated with the incidence of COVID-19 across 207 location-months, representing 23 geographic locations across 9 months; only 2% of chilblains cases were confirmed as potentially secondary to COVID-19.
>
> Meaning  The findings of this study suggest that the weak correlation between incidence of chilblains and incidence of COVID-19 infection may represent changes in pandemic behavior that led to increased diagnosis of chilblains."

*Transplant Patients*

Clin Infect Dis: Poor Antibody Response after Two Doses of SARS-CoV-2 vaccine in Transplant Recipients (24 June 2021)

> "A low anti-spike antibody response of 28.6% was observed 28 days after BNT162b2 vaccine second dose among 133 solid organ transplant-recipients without previous COVID-19. No serious adverse events were recorded. Four severe COVID-19 cases were reported between or after the two doses. Our data suggests to change the vaccine strategy."

NEJM: Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients (23 June 2021)

> "Here, we report the humoral response in a group of 101 consecutive solid-organ transplant recipients (mean [±SD] age, 58±2 years; 69% were men) who were given three doses of the

> messenger RNA vaccine BNT162b2 (Pfizer–BioNTech). The group included 78 kidney-transplant recipients, 12 liver-transplant recipients, 8 lung-transplant or heart-transplant recipients, and 3 pancreas-transplant recipients….
>
> This study showed that administration of a third dose of the BNT162b2 vaccine to solid-organ transplant recipients significantly improved the immunogenicity of the vaccine, with no cases of Covid-19 reported in any of the patients. However, a large proportion of the patients remain at risk for Covid-19. Barrier measures should be maintained, and vaccination of the relatives of these patients should be encouraged."

## Long COVID / Post-COVID Period

### *News in Brief*

Data from the UK-based REACT study suggest that more than 2 million people in England may have suffered from long COVID (BBC; see also: preprint from Imperial College London).

### *Peer-Reviewed Articles*

Nat Med: Long COVID in a prospective cohort of home-isolated patients (23 June 2021)

> "Long-term complications after coronavirus disease 2019 (COVID-19) are common in hospitalized patients, but the spectrum of symptoms in milder cases needs further investigation. We conducted a long-term follow-up in a prospective cohort study of 312 patients—247 home-isolated and 65 hospitalized—comprising 82% of total cases in Bergen during the first pandemic wave in Norway. At 6 months, 61% (189/312) of all patients had persistent symptoms, which were independently associated with severity of initial illness, increased convalescent antibody titers and pre-existing chronic lung disease. We found that 52% (32/61) of home-isolated young adults, aged 16–30 years, had symptoms at 6 months, including loss of taste and/or smell (28%, 17/61), fatigue (21%, 13/61), dyspnea (13%, 8/61), impaired concentration (13%, 8/61) and memory problems (11%, 7/61). Our findings that young, home-isolated adults with mild COVID-19 are at risk of long-lasting dyspnea and cognitive symptoms highlight the importance of infection control measures, such as vaccination."

### *Adverse Effects*

JAMA Netw Open: Clinical Outcomes for Patients With Anosmia 1 Year After COVID-19 Diagnosis (24 June 2021)

> "This cohort study examines the clinical course and prognosis of patients with COVID-19–related anosmia for 1 year after diagnosis….
>
> More than 1 year into the pandemic, we describe the long-term prognosis for a cohort of patients with COVID-19–related anosmia, most of whom (96.1%) objectively recovered by 12 months. Our findings suggest that an additional 10% gain in recovery can be expected at 12 months, compared with studies with 6 months of follow-up that found only 85.9% of patients with recovery. This supports findings from fundamental animal research, involving both imaging studies and postmortem pathology, suggesting that COVID-19–related anosmia is likely due to peripheral inflammation."

JAMA Otolaryngol Head Neck Surg: Incidence of Bell Palsy in Patients With COVID-19 (24 June 2021)

> "This cohort study compares the incidence of Bell palsy among patients with COVID-19 and those vaccinated against the disease….
>
> The present analysis found a higher incidence of BP [Bell palsy] in patients with COVID-19 (0.08%). This translates to approximately 82 per 100 000 patients with COVID-19. The rate of recurrent BP in patients with previous BP at the time of COVID-19 diagnosis was 8.6%. This analysis found a statistically significant higher risk of BP in patients with COVID-19 compared with those who were vaccinated against the disease. The data suggest that rates of BP are higher in patients with COVID-19, and this incidence exceeds the reported incidence of BP in those who have received a COVID-19 vaccine."

## Women's Health, Pregnancy, and Perinatal Care

### ***News in Brief***

"COVID vaccines and breastfeeding: what the data say: The vaccines do not pass through breastmilk, but antibodies do — providing hope that breastfed babies might have some level of protection" (Nature).

### *Peer-Reviewed Articles*

NEJM: Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons (17 June 2021)

> "Background: Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy.
>
> Methods: From December 14, 2020, to February 28, 2021, we used data from the "v-safe after vaccination health checker" surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons.
>
> Results: A total of 35,691 v-safe participants 16 to 54 years of age identified as pregnant. Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. Among 3958 participants enrolled in the v-safe pregnancy registry, 827 had a completed pregnancy, of which 115 (13.9%) resulted in a pregnancy loss and 712 (86.1%) resulted in a live birth (mostly among participants with vaccination in the third trimester). Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%); no neonatal deaths were reported. Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases).
>
> Conclusions: Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes."

## Pediatric Population

### *News in Brief*

"85 teens, staffers get coronavirus at summer camp that didn’t require masks or check vaccine status" (WP).

***Peer-Reviewed Articles***

MMWR: Disparities in Learning Mode Access Among K–12 Students During the COVID-19 Pandemic, by Race/Ethnicity, Geography, and Grade Level — United States, September 2020–April 2021 (02 July 2021)

> "What is already known about this topic? Reduced access to in-person learning is associated with poorer learning outcomes and adverse mental health and behavioral effects in children.
>
> What is added by the report? Although access to in-person, hybrid, and virtual learning modes varied throughout the school year, during January–April 2021, access to full-time in-person learning for non-Hispanic White students increased by 36.6 percentage points, 31.1 percentage points for non-Hispanic Black students, 22.0 percentage points for Hispanic students, and 26.6 percentage points for students of other race/ethnicities.
>
> What are the implications for public health practice? To increase equitable access to full-time in-person learning for the 2021–22 school year, school leaders should focus on providing safety-optimized in-person learning options across grade levels in all geographic areas. Vaccination and other efforts to reduce levels of community transmission should be intensified."

Lancet Infect Dis: Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy children and adolescents: a double-blind, randomised, controlled, phase 1/2 clinical trial (28 June 2021)

> "Background A vaccine against SARS-CoV-2 for children and adolescents will play an important role in curbing the COVID-19 pandemic. Here we aimed to assess the safety, tolerability, and immunogenicity of a candidate COVID-19 vaccine, CoronaVac, containing inactivated SARS-CoV-2, in children and adolescents aged 3–17 years.
>
> Methods We did a double-blind, randomised, controlled, phase 1/2 clinical trial of CoronaVac in healthy children and adolescents aged 3–17 years old at Hebei Provincial Center for Disease Control and Prevention in Zanhuang (Hebei, China). Individuals with SARS-CoV-2 exposure or infection history were excluded. Vaccine (in 0·5 mL aluminum hydroxide adjuvant) or aluminum hydroxide only (alum only, control) was given by intramuscular injection in two doses (day 0 and day 28).
>
> We did a phase 1 trial in 72 participants with an age de-escalation in three groups and dose-escalation in two blocks (1·5 μg or 3·0 μg per injection). Within each block, participants were randomly assigned (3:1) by means of block randomisation to receive CoronaVac or alum only. In phase 2, participants were randomly assigned (2:2:1) by means of block randomisation to receive either CoronaVac at 1·5 μg or 3·0 μg per dose, or alum only. All participants, investigators, and laboratory staff were masked to group allocation. The

> primary safety endpoint was adverse reactions within 28 days after each injection in all participants who received at least one dose. The primary immunogenicity endpoint assessed in the per-protocol population was seroconversion rate of neutralising antibody to live SARS-CoV-2 at 28 days after the second injection. This study is ongoing and is registered with ClinicalTrials.gov, NCT04551547.
>
> Findings Between Oct 31, 2020, and Dec 2, 2020, 72 participants were enrolled in phase 1, and between Dec 12, 2020, and Dec 30, 2020, 480 participants were enrolled in phase 2. 550 participants received at least one dose of vaccine or alum only (n=71 for phase 1 and n=479 for phase 2; safety population). In the combined safety profile of phase 1 and phase 2, any adverse reactions within 28 days after injection occurred in 56 (26%) of 219 participants in the 1·5 μg group, 63 (29%) of 217 in the 3·0 μg group, and 27 (24%) of 114 in the alum-only group, without significant difference (p=0·55).
>
> Most adverse reactions were mild and moderate in severity. Injection site pain was the most frequently reported event (73 [13%] of 550 participants), occurring in 36 (16%) of 219 participants in the 1·5 μg group, 35 (16%) of 217 in the 3·0 μg group, and two (2%) in the alum-only group. As of June 12, 2021, only one serious adverse event of pneumonia has been reported in the alum-only group, which was considered unrelated to vaccination. In phase 1, seroconversion of neutralising antibody after the second dose was observed in 27 of 27 participants (100·0% [95% CI 87·2–100·0]) in the 1·5 μg group and 26 of 26 participants (100·0% [86·8-100·0]) in the 3·0 μg group, with the geometric mean titres of 55·0 (95% CI 38·9–77·9) and 117·4 (87·8–157·0). In phase 2, seroconversion was seen in 180 of 186 participants (96·8% [93·1–98·8]) in the 1·5 μg group and 180 of 180 participants (100·0% [98·0–100·0]) in the 3·0 μg group, with the geometric mean titres of 86·4 (73·9–101·0) and 142·2 (124·7–162·1). There were no detectable antibody responses in the alum-only groups.
>
> Interpretation CoronaVac was well tolerated and safe and induced humoral responses in children and adolescents aged 3–17 years. Neutralising antibody titres induced by the 3·0 μg dose were higher than those of the 1·5 μg dose. The results support the use of 3·0 μg dose with a two-immunisation schedule for further studies in children and adolescents."

JAMA Pediatr: Association Between Race and COVID-19 Outcomes Among 2.6 Million Children in England (21 June 2021)

> "Question Is race associated with COVID-19 testing and hospital outcomes in children in England?
>
> Findings In this cohort study of 2 576 353 children (0-18 years of age) in England with COVID-19 disease, children who were Black, Asian, or of mixed race had lower proportions of SARS-CoV-2 tests and had higher positive results and COVID-19 hospitalizations

> compared with White children. These results held after key demographic factors and selected comorbidities were accounted for.
>
> Meaning These findings suggest that race may play an important role in childhood COVID-19 outcomes, which reinforces the continued need for a race-tailored focus on health system performance and targeted public health interventions."

NEJM: Multisystem Inflammatory Syndrome in Children — Initial Therapy and Outcomes (01 July 2021; online) 16 June 2021)

> "Background: The assessment of real-world effectiveness of immunomodulatory medications for multisystem inflammatory syndrome in children (MIS-C) may guide therapy.
>
> Methods: We analyzed surveillance data on inpatients younger than 21 years of age who had MIS-C and were admitted to 1 of 58 U.S. hospitals between March 15 and October 31, 2020. The effectiveness of initial immunomodulatory therapy (day 0, indicating the first day any such therapy for MIS-C was given) with intravenous immune globulin (IVIG) plus glucocorticoids, as compared with IVIG alone, was evaluated with propensity-score matching and inverse probability weighting, with adjustment for baseline MIS-C severity and demographic characteristics. The primary outcome was cardiovascular dysfunction (a composite of left ventricular dysfunction or shock resulting in the use of vasopressors) on or after day 2. Secondary outcomes included the components of the primary outcome, the receipt of adjunctive treatment (glucocorticoids in patients not already receiving glucocorticoids on day 0, a biologic, or a second dose of IVIG) on or after day 1, and persistent or recurrent fever on or after day 2.
>
> Results: A total of 518 patients with MIS-C (median age, 8.7 years) received at least one immunomodulatory therapy; 75% had been previously healthy, and 9 died. In the propensity-score-matched analysis, initial treatment with IVIG plus glucocorticoids (103 patients) was associated with a lower risk of cardiovascular dysfunction on or after day 2 than IVIG alone (103 patients) (17% vs. 31%; risk ratio, 0.56; 95% confidence interval [CI], 0.34 to 0.94). The risks of the components of the composite outcome were also lower among those who received IVIG plus glucocorticoids: left ventricular dysfunction occurred in 8% and 17% of the patients, respectively (risk ratio, 0.46; 95% CI, 0.19 to 1.15), and shock resulting in vasopressor use in 13% and 24% (risk ratio, 0.54; 95% CI, 0.29 to 1.00). The use of adjunctive therapy was lower among patients who received IVIG plus glucocorticoids than among those who received IVIG alone (34% vs. 70%; risk ratio, 0.49; 95% CI, 0.36 to 0.65), but the risk of fever was unaffected (31% and 40%, respectively; risk ratio, 0.78; 95% CI, 0.53 to 1.13). The inverse-probability-weighted analysis confirmed the results of the propensity-score-matched analysis.

> Conclusions: Among children and adolescents with MIS-C, initial treatment with IVIG plus glucocorticoids was associated with a lower risk of new or persistent cardiovascular dysfunction than IVIG alone."
>
> See also: editorial

NEJM: Treatment of Multisystem Inflammatory Syndrome in Children (01 July 2021; online) 16 June 2021)

> "Background: Evidence is urgently needed to support treatment decisions for children with multisystem inflammatory syndrome (MIS-C) associated with severe acute respiratory syndrome coronavirus 2.
>
> Methods: We performed an international observational cohort study of clinical and outcome data regarding suspected MIS-C that had been uploaded by physicians onto a Web-based database. We used inverse-probability weighting and generalized linear models to evaluate intravenous immune globulin (IVIG) as a reference, as compared with IVIG plus glucocorticoids and glucocorticoids alone. There were two primary outcomes: the first was a composite of inotropic support or mechanical ventilation by day 2 or later or death; the second was a reduction in disease severity on an ordinal scale by day 2. Secondary outcomes included treatment escalation and the time until a reduction in organ failure and inflammation.
>
> Results: Data were available regarding the course of treatment for 614 children from 32 countries from June 2020 through February 2021; 490 met the World Health Organization criteria for MIS-C. Of the 614 children with suspected MIS-C, 246 received primary treatment with IVIG alone, 208 with IVIG plus glucocorticoids, and 99 with glucocorticoids alone; 22 children received other treatment combinations, including biologic agents, and 39 received no immunomodulatory therapy. Receipt of inotropic or ventilatory support or death occurred in 56 patients who received IVIG plus glucocorticoids (adjusted odds ratio for the comparison with IVIG alone, 0.77; 95% confidence interval [CI], 0.33 to 1.82) and in 17 patients who received glucocorticoids alone (adjusted odds ratio, 0.54; 95% CI, 0.22 to 1.33). The adjusted odds ratios for a reduction in disease severity were similar in the two groups, as compared with IVIG alone (0.90 for IVIG plus glucocorticoids and 0.93 for glucocorticoids alone). The time until a reduction in disease severity was similar in the three groups.
>
> Conclusions: We found no evidence that recovery from MIS-C differed after primary treatment with IVIG alone, IVIG plus glucocorticoids, or glucocorticoids alone, although significant differences may emerge as more data accrue."
>
> See also: editorial

## Impact on Healthcare Workers

### *News in Brief*

Opinion: "The health care workforce is understaffed for life after Covid-19" (STAT).

Long read: "The doctors are not all right: Doctors need mental health support, but the medical profession often punishes them for getting it" (Vox).

### *Peer-Reviewed Articles*

MMWR: Symptoms of Depression, Anxiety, Post-Traumatic Stress Disorder, and Suicidal Ideation Among State, Tribal, Local, and Territorial Public Health Workers During the COVID-19 Pandemic — United States, March–April 2021 (02 July 2021)

> "What is already known about this topic? Increases in mental health conditions have been documented among the general population and health care workers during the COVID-19 pandemic; however, data on public health workers are limited.
>
> What is added by this report? Among 26,174 surveyed state, tribal, local, and territorial public health workers, 53.0% reported symptoms of at least one mental health condition in the past 2 weeks. Symptoms were more prevalent among those who were unable to take time off or worked ≥41 hours per week.
>
> What are the implications for public health practice? Implementing prevention and control practices that eliminate, reduce, and manage factors that cause or contribute to public health workers' poor mental health might improve mental health outcomes during emergencies."

JAMA Netw Open: Changes in Physician Work Hours and Patterns During the COVID-19 Pandemic (23 June 2021)

> "This study examines the hours worked and patterns of work activities before and during the COVID-19 pandemic among US physicians….
>
> This study found that physicians' work hours have significantly decreased since the start of the COVID-19 pandemic in the US, accelerating an existing, gradual decline. There was also a decreased percentage of physicians working full-time, a rise in the percentage who were laid off, and increased changes in physicians' usual activities. These observed changes may reflect the decrease in health care utilization and the increased flexibilities instigated by COVID-19–driven regulations. The decline in the percentage of parents with preschool-aged children among only female physicians may suggest a disproportionate uptake of childcare responsibilities among female physicians."

Clin Infect Dis: Strong SARS-CoV-2-neutralizing antibody response of previously-infected healthcare workers given one dose of mRNA vaccine (22 June 2021)

> "We followed up 195 healthcare workers (HCWs) who tested positive with a quantitative enzyme-linked immunosorbent assay (ELISA) after the first epidemic wave (10 June-10 July, 2020). Their neutralizing antibody titers were determined with a virus neutralisation assay [5]. About one fifth (40, 20.5%) of them were vaccinated after January 2021, and 30 (15.4%) were given a single dose of the Pfizer vaccine. We set up matched pairs (age and gender) of HCWs: infected/unvaccinatedon April 2021 and uninfected/vaccinate (2 doses of Pfizer mRNA vaccine…
>
> These data indicate that an initial SARS-CoV-2 infection that is not followed by vaccination confers less immunity than does vaccination alone. Nevertheless, the immunity developed by infected/vaccinated (single dose) HCWs is greater than that developed by uninfected/vaccinated (2 doses) HCWs."

JAMA Netw Open: SARS-CoV-2 Positivity and Mask Utilization Among Health Care Workers (22 June 2021)

> "This cohort study examines the association of mask use with COVID-19 transmission among health care workers in California….
>
> Our study found no association in positivity rates among HCW [health care workers] wearing RM [respirator masks] vs MM [medical masks] when performing nonaerosolizing, routine patient care, supporting findings from a recent case-control study and an earlier case report suggesting that MM protected HCWs from acquiring COVID-19. Only 4 positive tests followed exposure events (2 among nursing staff, 2 among technician staff), none were from confirmed AEs, and all occurred prior to universal masking implementation. More than 95% of HCWs acquired COVID-19 outside of a known patient-related exposure event, possibly due to improper donning and doffing of masks during social interactions with other HCWs in the workplace or in the community, supporting a study finding higher risk of COVID-19 transmission outside of patient care interactions."

## Mental Health, Psychosocial Issues, and Wellness

### *News in Brief*

Everyone's mental health has taken a hit during the pandemic; kids in crisis are languishing in ERs for days (NPR), grad students are often overlooked (Nature), and people are urgently looking for mental health support (WSJ).

"By now, burnout is a given: The pandemic has stripped our emotional reserves even further, laying bare our unique physical, social, and emotional vulnerabilities" (Atlantic).

"Stuck in a rut? Sometimes joy takes a little practice" (NPR). If you need some guidance, try NPR's Joy Generator (headphones suggested). Personally, I'm a fan of the sound of a steady rain or ocean waves (I use the Calm app for that when nature doesn't provide it) and watching this video of the northern lights on repeat (or you can try this 2-hour version).

### *Peer-Reviewed Articles*

BMC Fam Pract: Primary care teams' experiences of delivering mental health care during the COVID-19 pandemic: a qualitative study (01 July 2021)

> "Background: Integrated primary care teams are ideally positioned to support the mental health care needs arising during the COVID-19 pandemic. Understanding how COVID-19 has affected mental health care delivery within primary care settings will be critical to inform future policy and practice decisions during the later phases of the pandemic and beyond. The objective of our study was to describe the impact of the COVID-19 pandemic on primary care teams' delivery of mental health care.
>
> Methods: A qualitative study using focus groups conducted with primary care teams in Ontario, Canada. Focus group data was analysed using thematic analysis.
>
> Results: We conducted 11 focus groups with 10 primary care teams and a total of 48 participants. With respect to the impact of the COVID-19 pandemic on mental health care in primary care teams, we identified three key themes: i) the high demand for mental health care, ii) the rapid transformation to virtual care, and iii) the impact on providers.
>
> Conclusions: From the outset of the COVID-19 pandemic, primary care quickly responded to the rising mental health care demands of their patients. Despite the numerous challenges they faced with the rapid transition to virtual care, primary care teams have persevered. It is essential that policy and decision-makers take note of the toll that these demands have placed on providers. There is an immediate need to enhance primary care's capacity for mental health care for the duration of the pandemic and beyond."

JAMA Netw Open: Lived Experiences of Family Members of Patients With Severe COVID-19 Who Died in Intensive Care Units in France (21 June 2021)

> "Question What is the experience of bereaved family members after the death of a loved one in an intensive care unit (ICU) during the first wave of the COVID-19 pandemic?
>
> Findings In this qualitative study of 19 bereaved family members, participants reported difficulties in establishing a bond with the ICU team and maintaining a relationship with

> their loved ones during their stay in the ICU. They also described a feeling of “stolen moments” after the death of their loved one, generating strong feelings of disbelief that could potentially lead to complicated grieving.
>
> Meaning  These findings suggest that while adapting care practices and visiting policies is necessary given the public health menace, preventing families from seeing their loved ones altogether was highly detrimental: specific family-centered guidelines for crisis management are needed."
>
> See also: invited commentary

**Disparities and Health Equity**

***News in Brief***

"'Nobody is catching it': Algorithms used in health care nationwide are rife with bias" (STAT).

***Peer-Reviewed Articles***

JAMA Netw Open: Assessment of Racial and Ethnic Disparities in Access to COVID-19 Vaccination Sites in Brooklyn, New York (18 June 2021)

> "This cross-sectional study examines the number and location of vaccination sites across 18 districts with varying racial and ethnic demographic characteristics in Brooklyn, New York….
>
> The findings of this study suggest that there are substantial vaccination access deserts (areas without ample vaccination resources relative to surrounding areas). With many preliminary barriers to vaccination uptake, including supply issues, scheduling multiple doses, and a delay for scheduling appointments, vaccine rollout has been slow. Furthermore, early COVID-19 vaccination efforts in NYC have been focused primarily in White, middle-to-upper class neighborhoods, with the greatest access occurring in these areas."

Int J Environ Res Public Health: Lockdown-Related Disparities Experienced by People with Disabilities during the First Wave of the COVID-19 Pandemic: Scoping Review with Thematic Analysis (08 June 2021)

> "People with disabilities may be disproportionally affected by the COVID-19 pandemic. We synthesize the literature on broader health and social impacts on people with disabilities arising from lockdown-related measures. Methods: Scoping review with thematic analysis. Up to mid-September 2020, seven scientific databases and three pre-print servers were

> searched to identify empirical or perspective papers addressing lockdown-related disparities experienced by people with disabilities. Snowballing searches and experts' consultation also occurred. Two independent reviewers took eligibility decisions and performed data extractions. Results: Out of 1026 unique references, 85 addressed lockdown-related disparities experienced by people with disabilities. Ten primary and two central themes were identified: (1) Disrupted access to healthcare (other than for COVID-19); (2) Reduced physical activity leading to health and functional decline; (3) From physical distance and inactivity to social isolation and loneliness; (4) Disruption of personal assistance and community support networks; (5) Children with disabilities disproportionally affected by school closures; (6) Psychological consequences of disrupted routines, activities, and support; (7) Family and informal caregiver burden and stress; (8) Risks of maltreatment, violence, and self-harm; (9) Reduced employment and/or income exacerbating disparities; and (10) Digital divide in access to health, education, and support services. Lack of disability-inclusive response and emergency preparedness and structural, pre-pandemic disparities were the central themes. Conclusions: Lockdown-related measures to contain the COVID-19 pandemic can disproportionally affect people with disabilities with broader impact on their health and social grounds. Lack of disability-inclusive response and emergency preparedness and pre-pandemic disparities created structural disadvantages, exacerbated during the pandemic. Both structural disparities and their pandemic ramifications require the development and implementation of disability-inclusive public health and policy measures."

## Risk, Transmission, Exposure, and Serosurveillance

### *News in Brief*

"Your pets can catch Covid from you, and cats appear more susceptible than dogs: The more time a cat spent with its owner, the higher the risk of infection, new research finds" (NBC).

"Sewage sleuths helped an Arizona town beat back Covid-19. For wastewater epidemiology, that's just the start" (STAT).

### *Peer-Reviewed Articles*

J infect Dis: Longitudinal assessment of diagnostic test performance over the course of acute SARS-CoV-2 infection (30 June 2021)

> "Background: Serial screening is critical for restricting spread of SARS-CoV-2 by facilitating the timely identification of infected individuals to interrupt transmission chains. The

> variation in sensitivity of different diagnostic tests at different stages of infection has not been well documented.
>
> Methods: This is a longitudinal study of 43 adults newly infected with SARS-CoV-2. All participants provided daily samples for saliva and nasal swab RTqPCR, Quidel SARS Sofia antigen FIA, and live virus culture.
>
> Results: We show that both RTqPCR and the Quidel SARS Sofia antigen FIA peak in sensitivity during the period in which live virus is detected in nasal swabs, but the sensitivity of RTqPCR tests rises more rapidly prior to this period. We also estimate the sensitivities of RTqPCR and antigen tests as a function of testing frequency.
>
> Conclusions: RTqPCR tests are more effective than antigen tests at identifying infected individuals prior to or early during the infectious period and thus for minimizing forward transmission (given timely results reporting). All tests showed >98% sensitivity for identifying infected individuals if used at least every three days. Daily screening using antigen tests can achieve ~90% sensitivity for identifying infected individuals while they are viral culture positive."

Clin Infect Dis: Characterization of SARS-CoV-2 infection clusters based on integrated genomic surveillance, outbreak analysis and contact tracing in an urban setting (28 June 2021)

> "Background: Tracing of SARS-CoV-2 transmission chains is still a major challenge for public health authorities, when incidental contacts are not recalled or are not perceived as potential risk contacts. Viral sequencing can address key questions about SARS-CoV-2 evolution and may support reconstruction of viral transmission networks by integration of molecular epidemiology into classical contact tracing.
>
> Methods: In collaboration with local public health authorities, we set up an integrated system of genomic surveillance in an urban setting, combining a) viral surveillance sequencing, b) genetically based identification of infection clusters in the population, c) integration of public health authority contact tracing data, and d) a user-friendly dashboard application as a central data analysis platform.
>
> Results: Application of the integrated system from August to December 2020 enabled a characterization of viral population structure, analysis of four outbreaks at a maximum care hospital, and genetically based identification of five putative population infection clusters, all of which were confirmed by contact tracing. The system contributed to the development of improved hospital infection control and prevention measures and enabled the identification of previously unrecognized transmission chains, involving a martial arts gym and establishing a link between the hospital to the local population.
>
> Conclusions: Integrated systems of genomic surveillance could contribute to the monitoring and, potentially, improved management of SARS-CoV-2 transmission in the population."

Nat Biotechnol: Wearable materials with embedded synthetic biology sensors for biomolecule detection (28 June 2021)

> "Integrating synthetic biology into wearables could expand opportunities for noninvasive monitoring of physiological status, disease states and exposure to pathogens or toxins. However, the operation of synthetic circuits generally requires the presence of living, engineered bacteria, which has limited their application in wearables. Here we report lightweight, flexible substrates and textiles functionalized with freeze-dried, cell-free synthetic circuits, including CRISPR-based tools, that detect metabolites, chemicals and pathogen nucleic acid signatures. The wearable devices are activated upon rehydration from aqueous exposure events and report the presence of specific molecular targets by colorimetric changes or via an optical fiber network that detects fluorescent and luminescent outputs. The detection limits for nucleic acids rival current laboratory methods such as quantitative PCR. We demonstrate the development of a face mask with a lyophilized CRISPR sensor for wearable, noninvasive detection of SARS-CoV-2 at room temperature within 90 min, requiring no user intervention other than the press of a button."

JAMA Netw Open: Utility of Mass SARS-CoV-2 Testing of Asymptomatic Patients Before Ambulatory and Inpatient Preplanned Procedures Requiring Moderate Sedation or General Anesthesia (25 June 2021)

> "This quality improvement study describes the results of a mass preprocedure SARS-CoV-2 testing strategy during a period of high community transmission in Connecticut….
>
> With preprocedure testing, we detected asymptomatic patients with SARS-CoV-2 who were missed by clinical screening alone. Testing programs like this one can reduce potential transmission events while providing an additional layer of HCP safety. Postprocedural infectious complications of COVID-19 in this higher-risk population are also mitigated when COVID-19 status is known and procedural delay is possible. Additionally, the resource burden of performing procedures using COVID-19 precautions is reduced.
>
> The optimal timing for preprocedural testing is unknown."

MMWR: COVID-19 Surveillance and Investigations in Workplaces — Seattle & King County, Washington, June 15–November 15, 2020 (25 June 2021)

> "What is already known about this topic? Workplace activities that involve close contact with coworkers and customers can lead to COVID-19 spread.
>
> What is added by this report? Workplace investigations were prioritized using workplace features associated with increased COVID-19 spread and with severe disease outcomes. High-priority investigations were more likely than were medium- and low-priority investigations to have two or more cases among employees, two or more cases not

> previously linked to the workplace, or two or more exposed workplace contacts not previously elicited during case interviews.
>
> What are the implications for public health practice? Workplace investigations uncovered contacts not previously elicited and cases not previously linked to the workplace, demonstrating the importance of conducting workplace investigations in addition to routine case interviews to limit the potential workplace spread of COVID-19."

J Infect Dis: Detection of serum cross-reactive antibodies and memory response to SARS-CoV-2 in pre-pandemic and post-COVID-19 convalescent samples (23 June 2021)

> "Background: A notable feature of COVID-19 is that children are less susceptible to severe disease. Children are known to experience more infections with endemic human coronaviruses (HCoVs) compared to adults. Little is known whether HCoV infections lead to cross-reactive anti-SARS-CoV-2 antibodies.
>
> Methods: We investigated the presence of cross-reactive anti-SARS-CoV-2 IgG antibodies (to spike(S)1, S1-receptor-binding receptor (S1-RBD) and nucleocapsid protein(NP)), by enzyme-linked immunosorbent assays, and neutralizing activity by a SARS-CoV-2 pseudotyped virus neutralisation assay, in pre-pandemic sera collected from children(n=50) and adults(n=45), and compared with serum samples from convalescent COVID-19 patients(n=16).
>
> Results: A significant proportion of children (up to 40%) had detectable cross-reactive antibodies to SARS-CoV-2 S1, S1-RBD and NP antigens, and the anti-S1 and -S1-RBD antibody levels correlated with anti-HCoV-HKU1 and -OC43 S1 antibody titers in pre-pandemic samples(p<0.001). There were marked increases of anti-HCoV-HKU1 and -OC43 S1 (but not anti-NL63 and -229E S-RBD) antibody titres in serum samples from convalescent COVID-19 patients (p<0.001), indicating an activation of cross-reactive immunological memory to β-coronavirus spike.
>
> Conclusions: We demonstrated cross-reactive anti-SARS-CoV-2 antibodies in pre-pandemic serum samples from children and young adults. Promoting this cross-reactive immunity and memory response derived from common HCoV may be an effective strategy against SARS-COV-2 and future novel coronaviruses."

Sci Transl Med: Undiagnosed SARS-CoV-2 Seropositivity During the First Six Months of the COVID-19 Pandemic in the United States (22 June 2021)

> "Asymptomatic SARS-CoV-2 infection and delayed implementation of diagnostics have led to poorly defined viral prevalence rates in the United States and elsewhere. To address this, we analyzed seropositivity in 9,089 adults in the United States who had not been diagnosed previously with COVID-19. Individuals with characteristics that reflected the US population (n = 27,716) were selected by quota sampling from 462,949 volunteers. Enrolled

> participants (n = 11,382) provided medical, geographic, demographic, and socioeconomic information, and dried blood samples. Survey questions coincident with the Behavioral Risk Factor Surveillance System survey, a large probability-based national survey, were used to adjust for selection bias. The majority (88.7%) of blood samples were collected between May 10th and July 31st, 2020 and were processed using ELISA to measure seropositivity (IgG and IgM antibodies against SARS-CoV-2 spike protein and the spike protein receptor binding domain). The overall weighted undiagnosed seropositivity estimate was 4.6% (95% CI: 2.6-6.5%) with race, age, sex, ethnicity, and urban/rural subgroup estimates ranging from 1.1% to 14.2%; the highest seropositivity estimates were in African American participants, younger, female, and Hispanic participants, and residents of urban centers. These data indicate that there were 4.8 undiagnosed SARS-CoV-2 infections for every diagnosed case of COVID-19, and an estimated 16.8 million infections were undiagnosed by mid-July 2020 in the United States."

JAMA Intern Med: Assessing the Association Between Social Gatherings and COVID-19 Risk Using Birthdays (21 June 2021)

> "Question  Is there an association between household birthdays, which likely correspond to informal social gatherings, and COVID-19 infection?
>
> Findings  This cross-sectional study used administrative health care data on 2.9 million households from the first 45 weeks of 2020 and found that, among households in the top decile of county COVID-19 prevalence, those with birthdays had 8.6 more diagnoses per 10 000 individuals compared with households without a birthday, a relative increase of 31% of county-level prevalence, an increase in COVID-19 diagnoses of 15.8 per 10 000 persons after a child birthday, and an increase in COVID-19 diagnoses of 5.8 per 10 000 among households with an adult birthday.
>
> Meaning  This study suggests that events that lead to small and informal social gatherings, such as birthdays, and in particular, children’s birthdays, are a potentially important source in SARS-CoV-2 transmission."

Clin Infect Dis: The Risk of SARS-CoV-2 Transmission from Patients with Undiagnosed Covid-19 to Roommates in a Large Academic Medical Center (18 June 2021)

> "We assessed SARS-CoV-2 transmission between patients in shared rooms in an academic hospital between September 2020-April 2021. 11,290 patients were admitted to shared rooms, of whom 25 tested positive. Among 31 exposed roommates, 12 (39%) tested positive within 14 days. Transmission was associated with PCR cycle thresholds ≤21."

## Breakthrough Infections, Reinfections, and Coinfections

### *Peer-Reviewed Articles*

Clin Infect Dis: Variants of concern are overrepresented among post-vaccination breakthrough infections of SARS-CoV-2 in Washington State (24 June 2021)

> "Across 20 vaccine breakthrough cases detected at our institution, all 20 (100%) infections were due to variants of concern (VOC) and had a median Ct of 20.2 (IQR=17.1-23.3). When compared to 5174 contemporaneous samples sequenced in our laboratory, VOC were significantly enriched among breakthrough infections (p < .05)."

JAMA Intern Med: Association of Changes in Seasonal Respiratory Virus Activity and Ambulatory Antibiotic Prescriptions With the COVID-19 Pandemic (21 June 2021)

> "This pre-post study examines the association between respiratory virus incidence and ambulatory antibiotic orders and the COVID-19 pandemic….
>
> Consistent with our hypothesis, this study demonstrated a marked decrease in respiratory virus detections, with a concomitant 79% decline in ambulatory antibiotic prescribing rates for RTI [respiratory tract infections], during the COVID-19 pandemic. Prior studies conducted soon after the onset of the pandemic and over shorter durations showed relatively quick declines in rates of viral infections or antimicrobial prescribing. However, to our knowledge, this study is the first to combine respiratory virus activity and antibiotic prescriptions that were indexed to the number of encounters over a prolonged period that includes the typical respiratory virus season. The data suggest that COVID-19 transmission mitigation strategies may help curb respiratory viral diseases beyond SARS-CoV-2 and, indirectly, decrease antibiotic prescribing."

## Other Infectious Diseases

### *News in Brief*

"CDC investigating TB cases linked to tainted bone repair product used in more than 100 patients" (WP).

"A grisly skin disease is creeping into the American South: Flesh-eating parasites keep popping up in unexpected places" (Atlantic).

The CDC has warned of 3 cases of 'non-travel associated *Burkholderia pseudomallei* infections (melioidosis)' in the US (CDC).

New: focused update guidelines on the management of *C. diff* in adults (Clin Infect Dis).

The Ebola outbreak in Guinea has been declared over (WHO).

"Earliest known strain of plague could have come from a beaver bite: The disease may be 2000 years older than we thought" (Live Science).

*Malaria*

"It's official: China has eliminated malaria" (Science).

In other malaria news, 2 phase 1 trials of a malaria vaccine demonstrated 'strong, lasting protection' (NIH; see also: Nature paper).

### ***Peer-Reviewed Articles***

NEJM: Azithromycin or Doxycycline for Asymptomatic Rectal Chlamydia trachomatis (24 June 2021)

> "Background: Rectal chlamydia is a common bacterial sexually transmissible infection among men who have sex with men. Data from randomized, controlled trials are needed to guide treatment.
>
> Methods: In this double-blind trial conducted at five sexual health clinics in Australia, we randomly assigned men who have sex with men and who had asymptomatic rectal chlamydia to receive doxycycline (100 mg twice daily for 7 days) or azithromycin (1-g single dose). Asymptomatic chlamydia was selected as the trial focus because more than 85% of men with rectal chlamydia infection are asymptomatic, and clinical guidelines recommend a longer treatment course for symptomatic infection. The primary outcome was a negative nucleic acid amplification test for rectal chlamydia (microbiologic cure) at 4 weeks.
>
> Results: From August 2016 through August 2019, we enrolled 625 men (314 in the doxycycline group and 311 in the azithromycin group). Primary outcome data were available for 290 men (92.4%) in the doxycycline group and 297 (95.5%) in the azithromycin group. In the modified intention-to-treat population, a microbiologic cure occurred in 281 of 290 men (96.9%; 95% confidence interval [CI], 94.9 to 98.9) in the doxycycline group and in 227 of 297 (76.4%; 95% CI, 73.8 to 79.1) in the azithromycin group, for an adjusted risk difference of 19.9 percentage points (95% CI, 14.6 to 25.3; P<0.001). Adverse events that included nausea, diarrhea, and vomiting were reported in 98 men (33.8%) in the doxycycline group and in 134 (45.1%) in the azithromycin group (risk difference, -11.3 percentage points; 95% CI, -19.5 to -3.2).
>
> Conclusions: A 7-day course of doxycycline was superior to single-dose azithromycin in the treatment of rectal chlamydia infection among men who have sex with men."

## Statistics

*Global*
*02 JUL 2021:* 182,747,382 confirmed cases and 3,957,753 deaths

*Looking Back*
*30 JUN 2020:* 10,424,992 confirmed cases and 509,706 deaths in 188 countries/regions
(from: NMCP COVID-19 Literature Report #26)

*United States*

| | | top 5 states by cases | | | | |
|---|---|---|---|---|---|---|
| | TOTAL US | CA | TX | FL | NY | IL |
| Cases | 33,679,937 | 3,817,695 | 3,001,682 | 2,365,464 | 2,115,377 | 1,392,196 |
| Deaths | 605,036 | 63,712 | 52,410 | 37,772 | 53,690 | 25,670 |

JHU CSSE as of 1000 EDT 02 July 2021

| *Virginia* | Total (state) | Chesapeake | Hampton | Newport News | Norfolk | Portsmouth | Suffolk | Virginia Beach |
|---|---|---|---|---|---|---|---|---|
| Cases | 680,744 | 21,267 | 10,731 | 14,372 | 18,059 | 9,222 | 8,009 | 36,451 |
| Hospitalizations | 30,565 | 1,033 | 446 | 511 | 1,045 | 695 | 472 | 1,722 |
| Deaths | 11,423 | 307 | 182 | 239 | 272 | 204 | 192 | 416 |

VA DOH as of 1000 EDT 02 July 2021

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